REMARKS

Claims 1-3, 7-9 and 22-26 are currently pending. By this amendment, claims 1, 2, 3, 7, 8, 23, 24, 25 and 26 have been amended to specifically point out and distinctly claim that which the Applicants regard as the invention. In particular, claims 1 and 7 have been amended to recite a method for screening a compound wherein a purified or partially purified Cks1 is added to the reaction mixture. Claim 2 has been amended to correct a typographical error. Claim 3 has been amended to depend on claim 1. Claim 32 has been amended to recite, in part, a method for screening a compound comprising contacting a test compound in vitro which a reaction mixture comprising Skp2, p27, Cdk2 and Cks1, and detecting a change in Skp2 binding to Cks1. Claim 24 has been amended to depend on claim 23, wherein a decrease in the binding of Skp2 to Cks1 is detected. Claim 25, which is dependent on claim 2, has been amended to recite, in part, a method for screening a compound, wherein an increase in the binding of Skp2 to p27 is detected. Claim 26, which is dependent on claim 2, has been amended to recite, in part, a method for screening a compound, wherein a decrease in the binding of Skp2 to p27 is detected. New claims 27-33 have been added. Support for the amendments and new claims may be found in the specification, *inter alia*, on page 19, line 14 to page 20, line 14; page 58, line 1 to page 59, line 19; page 97, lines 16-27; page 103, line 26 to page 106, line 9 and the originally filed claims. As such, no new matter has been added. Claims 1-3, 7-9 and claims 22-33 will be pending upon entry of the instant amendment.

1. THE OBJECTION TO CLAIMS 23 AND 24 SHOULD BE WITHDRAWN

Claims 23 and 24 are objected to as being dependent upon a rejected base claim. The Examiner indicated that these claims would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims. In response, claim 23 has been amended to recite, in part, a method for screening a compound comprising contacting a test compound in vitro with a reaction mixture comprising Skp2, p27, Cdk2, and Cks1, and detecting a change in Skp2 binding to Cks1, such that if a change in Skp2 binding to Cks1 is detected, then a compound useful for the treatment of proliferative or differentiative disorders is identified. Claim 24 has been amended to depend on claim 23, wherein a decrease in the binding of Skp2 to Cks1 is detected. New claim 27, which is

dependent on claim 23, has been added to recite, wherein an increase in binding of Skp2 to Cks1 is detected. In addition, new claims 28-30 have been added. Claim 28 recites, in part, a method for screening comprising: (a) contacting a test compound with a reaction mixture containing Skp2, Cks1, and a polypeptide comprising the carboxyterminus of the human p27 chain; and (b) detecting a change in the binding of Skp2 to Cks1. Claim 29, which is dependent on claim 28, has been added to recite, a method wherein an increase in binding of Skp2 to Cks1 is detected. New claim 30, which is dependent on claim 28, has been added to recite, a method wherein a decrease in binding of Skp2 to Cks1 is detected. Thus, these claims are novel and non-obvious because they each specify a step for detecting a change in the binding of Skp 2 to Cks1, a newly identified protein. As such, Applicants submit that claims 23, 24, 27 and 28-30 are in condition for allowance.

2. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

The Examiner has rejected claim 22 under 35 U.S.C. § 112, second paragraph, for being indefinite. The Examiner contends that claim 22 requires that the Cks1 is purified from an *in vitro* translation reaction or recombinant expression system. The Examiner states that it is unclear if Applicant is intending to limit the claim to reaction mixtures having as a constituent *in vitro* purified Cks1. Applicants submit that claim 1 and 7 have been amended to recite, in part, a method for screening a compound, wherein a purified or partially purified Cks1 is added to the reaction mixture. As such, it is clear that claim 22, which depends on claim 1 or 7, limits the claim to recite, in part, a reaction mixture having as a constituent, purified or partially purified Cks1. Applicants therefore request that the rejection under 35 U.S.C. § 112 be withdrawn.

3. THE REJECTION UNDER 35 U.S.C. § 103(A) SHOULD BE WITHDRAWN

The Rejection Over Carrano As Evidenced By Ganoth

The Examiner has rejected claims 1-3, 7-9, 25 and 26 under 35 U.S.C. § 103(a) as being obvious over Carrano et al., 1999, Nature Cell Biology 1:193-199 ("Carrano") as evidenced by Ganoth et al., 2001, Nature Cell Biol 3:321-324 ("Ganoth"). The Examiner alleges that Carrano teaches that Skp2 is required for ubiquitin mediated degradation of p27 and that the addition of Skp1-Skp2 and cyclin E-CDK2 to G1 extracts of HeLa cells

stimulated p27 proteolysis. The Examiner further alleges that Carrano teaches that inhibitor of Skp2 should increase p27 and lead to a block in cellular proliferation. The Examiner also alleges that the HeLa cell extracts used by Carrano comprise Cks1 as evidenced by Ganoth, which teaches that Cks1 is present in HeLa cell extracts.

In response, claims 1 and 7 have been amended to recite, in part, a method for screening a compound wherein a purified or partially purified Cks1 is added to the reaction mixture. Support for the amendment may be found, *inter alia*, on page 59, lines 2-11. Thus, Carrano does not teach or suggest adding purified or partially purified Cks1 to the reaction mixture and therefore does not explicitly or inherently anticipate the present invention.

Claim 31 has been added to recite, in part, a method for screening a compound comprising contacting a test compound with a reaction mixture comprising Skp2, p27, Cdk2, and Cks1, and detecting a change in the binding of Skp2 to Cks1. Claim 32, which depends on claim 31, has been added to recite, wherein an increase in binding of Skp2 to Cks1 is detected. Claim 33, which depends on claim 31, has been added to recite, wherein a decrease in binding of Skp2 to Cks1 is detected. Applicants submit that these claims are not obvious over Carrano as evidenced by Ganoth. Rejection of these claims over 35 U.S.C. §103(a) should be withdrawn.

4. THE REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING SHOULD BE WITHDRAWN

Claims 1-3, 7-9, 25 and 26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-22 of copending Application No. 10/632,150 ('150 application) in view of Carrano. The Examiner contends that the claims are not patentably distinct from each other because claims 20 and 22 of the '150 application, in view of Carrano, would motivate one to detect the activity of Skp2 by measuring the ubiquitinination or proteolysis of p27.

Applicants submit that claims 20-22 of copending Application No. 10/632,150 have been canceled and are no longer pending. In addition, Applicant believes that the amendments made herein overcome the obviousness-type double patenting rejection for the same reasons as discussed above. Therefore, Applicants request that the rejection for obviousness-type double patenting be withdrawn.

CONCLUSION

Entry of the foregoing amendments and remarks into the record of the above-identified application is respectfully requested. Withdrawal of all rejections and reconsideration of the amended claims is requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

No additional fee is believed due with the filing of this response. However, should any additional fee be required, please charge any required fee to Jones Day Deposit Account No. 50-3013. A duplicate of this sheet is enclosed for accounting purposes.

Respectfully submitted,

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